

REMARKS

Status of the Claims

Claims 1 – 28 are pending, with claims 1, 12, 20, and 24 being independent. Without conceding the propriety of the rejections, claims 1, 5, 12, 14, 20, and 24 have been amended to even more clearly recite and distinctly claim the invention. Support for the amendments may be found throughout the specification including, for example, at page 3, paragraph [0011] and page 4, paragraph [0017]. Therefore, no new matter has been added.

Applicants respectfully request the Examiner to reconsider and withdraw the outstanding rejections in view of the foregoing amendments and the following remarks.

The Present Invention

The presently claimed invention relates to methods of inhibiting growth and reproduction of microorganisms in a cooling water system used in an industrial process. In the methods of the present invention, a deactivatable biocide and a neutralizing agent are used. The neutralizing agent is added to the water comprising the deactivatable biocide in an amount effective to *irreversibly* deactivate the biocide. The specification teaches that deactivation, according to the present invention, is an irreversible process, i.e., the process may not be reversed to re-generate the active biocide. (page 7 – 8, paragraph [0032]).

In certain embodiments, the presently claimed invention relates to integrated methods of inhibiting growth and reproduction of microorganisms in a cooling water system for a Fischer Tropsch facility. In the integrated process, a Fischer Tropsch synthesis is performed and Fischer Tropsch-derived liquid products and Fischer-Tropsch derived deactivatable biocides are isolated from the process. An effective amount of the Fischer-Tropsch derived biocide is added to the cooling water of the Fischer Tropsch process.

Claim rejections under 35 U.S.C. § 112

Claims 1-28 are rejected under 35 U.S.C. § 112, first paragraph for enablement. Applicants respectfully disagree with the rejection; therefore, this rejection is traversed.

Applicants respectfully submit that the specification is more than adequately enabling for the claimed scope of deactivatable biocides and neutralizing agents.

Applicants teach that a “deactivatable biocide” is a biocide that can be deactivated or neutralized once the danger of microbial growth has ended. (page 4, paragraph [0017]). Applicants specifically teach that the deactivatable biocides can be aldehydes or alkynes and provide examples. (page 8, paragraph [0034]). Applicants teach in detail how the aldehydes and alkynes act as biocides (page 8, paragraph [0034] – page 9, paragraph [0038]). With regard to the effective amount of the deactivatable biocides, Applicants teach that the biocides are added to cooling water in an amount effective to prevent visual growth of microorganisms for at least 10 days under ambient conditions when exposed to a certified inoculant. (pages 6–7, paragraphs [0030] – [0031]). Applicants provide an instrument and a method for measuring turbidity.

Applicants teach that a “neutralizing agent” is a compound or reaction conditions that may be used to react with a deactivatable biocide or to complex a deactivatable biocide to destroy the biocides’s antimicrobial activity. (pages 5-6, paragraph [0024]). Applicants further teach that the neutralizing agent irreversibly deactivates the biocide, i.e., the deactivatable biocide does not re-generate to become active upon release to the environment. (Id.) Applicants teach in detail how the neutralizing agent can be a nitrogen-containing compound selected from the group consisting of amines, amino acids, amino alcohols, and mixtures thereof when the biocide is an aldehyde or the neutralizing agent is a hydrogenation catalyst and H_2 when the biocide is an alkyne. (pages 10 – 11, paragraph [0043]).

With regard to the effective amount of neutralizing agent, the specification teaches that it is the amount to irreversibly deactivate the biocide. Applicants teach several ways in which to determine this effective amount. Applicants teach that the biocides and neutralizing agents may be measured in the cooling water by gas chromatography, wet chemical test, mass spectroscopy. Applicants also teach that small tests using mixtures of cooling water containing deactivatable biocide and neutralizing agent may be prepared and tested with certified inoculants to determine the optimum amount of neutralizing agent. (page 11, paragraph [0045]). Applicants further teach that in microbial growth tests, the cooling water containing deactivatable biocide with neutralizing agent added should support visible growth of microorganisms when exposed to a

certified inoculum within 10 days. Accordingly, the effective amount of the neutralizing agent is that amount that after added will provide water that supports visible growth of microorganisms when exposed to a certified inoculum within 10 days.

Applicants respectfully submit that more than adequate guidance in selecting and testing deactivatable biocides and neutralizing agents has been provided to enable one of ordinary skill in the art to practice the presently claimed invention. Applicants submit that test of enablement is not whether experimentation may be necessary. Applicants respectfully assert that a considerable amount of experimentation is permissible, if it is merely routine or if the specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Accordingly, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

Claim rejections under 35 U.S.C. § 103(a)

Claims 1-6 and 10-11 are rejected under 35 USC §103(a) as being obvious over Union Carbide in view of acknowledged prior art. Applicants respectfully disagree with the rejection; therefore, the rejection is traversed.

Union Carbide teaches that glutaraldehyde can be deactivated chemically by adding 2 –3 parts (by weight) of sodium bisulfite. (page 8). Union Carbide further teaches that the treated solutions of glutaraldehyde should be returned to neutral pH by the addition of an *inorganic acid*, e.g., hydrochloric acid, *before* disposal by appropriate means.

Applicants respectfully assert that the reaction of glutaraldehyde with sodium bisulfite is a *reversible* reaction. In support of the fact that the reaction is reversible, Applicants submit herewith Morrison and Boyd, *Organic Chemistry*, 2nd Edition, pages 639-641, a copy of which is attached. Morrison and Boyd teaches that “[s]odium bisulfite adds to most aldehydes and to many ketones ... to form bisulfite addition products.” Morrison and Boyd clearly teaches that “[l]ike other carbonyl addition reactions, this one is *reversible*.” Applicants further respectfully submit that adding an inorganic acid to the addition product of sodium bisulfite and glutaraldehyde regenerates the glutaraldehyde biocide. Morrison and Boyd clearly teaches that

“[a]ddition of acid or base destroys the bisulfite ion in equilibrium with the addition product, and regenerates the carbonyl compound.”

Accordingly, Union Carbide teaches a *reversible* deactivation of gluteraldehyde, and Union Carbide teaches *regenerating* the carbonyl compound by adding an inorganic acid *before* disposal by appropriate means.

In contrast, the presently claimed invention is directed to methods of inhibiting growth and reproduction of microorganisms in a cooling water system used in an industrial process. In the methods of the present invention, a deactivatable biocide and a neutralizing agent are used. The neutralizing agent is added to the water comprising the deactivatable biocide in an amount effective to *irreversibly* deactivate the biocide before or upon disposal of the cooling water. The specification teaches that deactivation, according to the present invention, is an *irreversible* process, i.e., the process may *not* be reversed to re-generate the active biocide. Applicants teach that irreversibly deactivating the deactivatable biocides according to the present invention advantageously avoids environmental and treatment concerns and eliminates the disposal and wastewater problems that accompany traditional use of biocides. (page 6, paragraph [0029]).

To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine the reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. MPEP § 2143.

It is respectfully submitted that in no way does Union Carbide disclose, teach, or suggest adding an effective amount of a neutralizing agent to the cooling water to *irreversibly* deactivate a biocide before or upon disposal of the cooling water. Applicants further respectfully submit that no art has been admitted that would supplement any deficiency of Union Carbide in this regard and the Examiner has not cited any documents to supplement the deficiency of Union Carbide in this regard. The Examiner is respectfully requested to provide a reference, provide evidence of these facts, or provide a detailed explanation as to why no evidence is required. MPEP §2144.03.

Since Union Carbide does not disclose, teach, or suggest adding an effective amount of a neutralizing agent to the cooling water to *irreversibly* deactivate the biocide and no art has been admitted or cited to supplement any deficiency of Union Carbide, Applicants respectfully request that the rejection be withdrawal

Claims 1-7, 9-17, and 19-23 are also rejected under 35 USC §103(a) as being obvious over Union Carbide in view of acknowledged prior art, Quann (U.S. Patent No. 4,686,317), and Hitzman (U.S. Patent No. 3,642,578). Applicants respectfully disagree with the rejection; therefore, this rejection is traversed.

As explained above, Union Carbide teaches *reversibly* deactivating gluteraldehyde by adding sodium bisulfite. Also as explained above, Union Carbide teaches *regenerating* the carbonyl compound by adding an inorganic acid *before* disposal by appropriate means.

Quann relates to a process for removing oxygenated impurities from a Fischer Tropsch hydrocarbon stream. In no way does Quann relate to or address biocides, microbial growth in cooling water, and/or environmental and treatment concerns for disposing of biocide treated water.

Hitzman relates to a process for microbial synthesis of cellular production products from oxygenated hydrocarbon feedstock containing aldehydes in addition to other oxygenated hydrocarbons comprising adding nitrogen-containing compounds to the feedstock. This process is used to produce proteins, amino acids, gums, and other valuable fermentation products. In no way does Hitzman relate to or address biocides, microbial growth in cooling water, and/or environmental and treatment concerns for disposing of biocide treated water.

In contrast, the presently claimed invention is directed to methods of inhibiting growth and reproduction of microorganisms in a cooling water system used in an industrial process. In the methods of the present invention, a deactivatable biocide and a neutralizing agent are used. The neutralizing agent is added to the water comprising the deactivatable biocide in an amount effective to *irreversibly* deactivate the biocide before or upon disposal of the cooling water.

In certain embodiments, the presently claimed invention relates to integrated methods of inhibiting growth and reproduction of microorganisms in a cooling water system for a Fischer Tropsch facility. In the integrated process, a Fischer Tropsch synthesis is performed and Fischer

Tropsch-derived liquid products and Fischer-Tropsch derived deactivatable biocides are isolated from the process. An effective amount of the Fischer-Tropsch derived biocide is added to the cooling water of the Fischer Tropsch process. The specification teaches that the integrated Fischer Tropsch processes of the present invention provide many benefits, as described at, for example, page 15, paragraph [0057] and page 16, paragraph [0060].

To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine the reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. MPEP § 2143.

Applicants respectfully submit that there is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine Union Carbide, Quann, and Hitzman. The teachings of Union Carbide do not suggest or provide any motivation to combine any feature of Union Carbide with Quann or Hitzman. Union Carbide is an industrial manual related to glutaraldehyde. Quann relates to removing impurities from a Fischer Tropsch process with no teaching or suggestion of biocides, microbial growth in cooling water, and/or environmental and treatment concerns for disposing of biocide treated water. Hitzman relates to producing proteins, amino acids, gums, and other valuable fermentation products from oxygenated hydrocarbon feedstocks with no teaching or suggestion of biocides, microbial growth in cooling water, and/or environmental and treatment concerns for disposing of biocide treated water.

Accordingly, Applicants respectfully submit that these documents are significantly different areas of technology and there is *no* suggestion or motivation to combine Union Carbide, Quann, and Hitzman. The Office Action has merely attempted to abstract individual teachings from the different pieces of prior art to create the combination upon which the rejection of the present claims was based. This is an error as a matter of law. *W.L. Gore & Associates v. Garlock, Inc.*, 721 F.2d 1540, 1552, 220 USPQ 303 312 (Fed. Cir. 1983).

Further, Applicants respectfully submit that even if there were some suggestion or motivation to combine the reference teachings and a reasonable expectation of success, the prior

art references when combined do not teach or suggest all the claim limitations. Even if combined, it is respectfully submitted that Union Carbide, Quann, and Hitzman do *not* teach or suggest adding an effective amount of a neutralizing agent to the cooling water to *irreversibly* deactivate the biocide before or upon disposal of the cooling water. It is further respectfully submitted that even if combined, Union Carbide, Quann, and Hitzman do *not* teach or suggest an integrated Fischer Tropsch process comprising isolating Fischer Tropsch derived deactivatable biocides and adding an effective amount of the Fischer Tropsch derived deactivatable biocides to the cooling water of the Fischer Tropsch process. In addition, even if combined, Union Carbide, Quann, and Hitzman do *not* teach or suggest an integrated Fischer Tropsch process comprising adding an effective amount of a neutralizing agent to the cooling water to *irreversibly* deactivate the Fischer-Tropsch derived deactivatable biocide before or upon disposal of the cooling water.

Applicants further respectfully submit that no art has been admitted that would supplement any deficiencies of the cited art in this regard and the Examiner has not cited any documents to supplement the deficiencies. The Examiner is respectfully requested to provide a reference, provide evidence of these facts, or provide a detailed explanation as to why no evidence is required. MPEP §2144.03.

Accordingly, it is respectfully submitted that even if the prior art references are combined, they do not teach or suggest all the claim limitations. Therefore, withdrawal of the obviousness rejections is respectfully requested.

Conclusion

Without conceding the propriety of the rejections, the claims have been amended, as provided above, to even more clearly recite and distinctly claim Applicants' invention and to pursue an early allowance. For the reasons noted above, the art of record does not disclose or suggest the inventive concept of the present invention as defined by the claims.

In view of the foregoing amendments and remarks, reconsideration of the claims and allowance of the subject application is earnestly solicited. The Examiner is invited to contact the undersigned at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted,

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ATTACHMENT A

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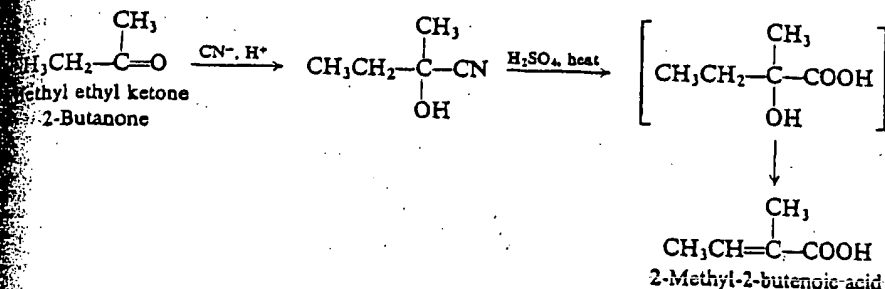
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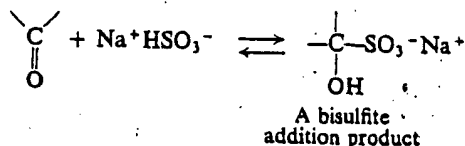


Problem 19.7 Each of the following is converted into the cyanohydrin, and the products are separated by careful fractional distillation or crystallization. For each reaction tell how many fractions will be collected, and whether each fraction, as collected, will be optically active or inactive, resolvable or non-resolvable.

- (a) Acetaldehyde; (b) benzaldehyde; (c) acetone;
 (d) R-(+)-glyceraldehyde, $\text{CH}_2\text{OHCHOHCHO}$; (e) (\pm) -glyceraldehyde.
 (f) How would your answer to each of the above be changed if each mixture were subjected to hydrolysis to hydroxy acids before fractionation?

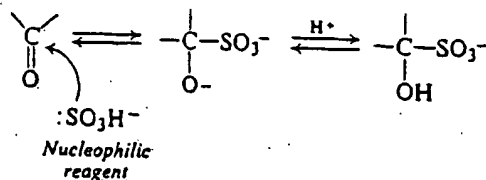
19.15 Addition of bisulfite

Sodium bisulfite adds to most aldehydes and to many ketones (especially methyl ketones) to form bisulfite addition products:

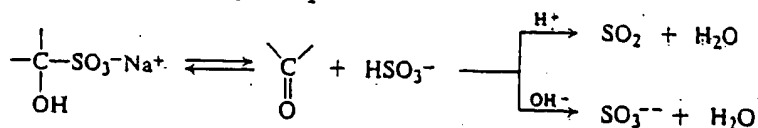


The reaction is carried out by mixing the aldehyde or ketone with a concentrated aqueous solution of sodium bisulfite; the product separates as a crystalline solid. Ketones containing bulky groups usually fail to react with bisulfite, presumably for steric reasons.

Addition involves nucleophilic attack by bisulfite ion on carbonyl carbon, followed by attachment of a hydrogen ion to carbonyl oxygen:



Like other carbonyl addition reactions, this one is reversible. Addition of acid or base destroys the bisulfite ion in equilibrium with the addition product, and regenerates the carbonyl compound.

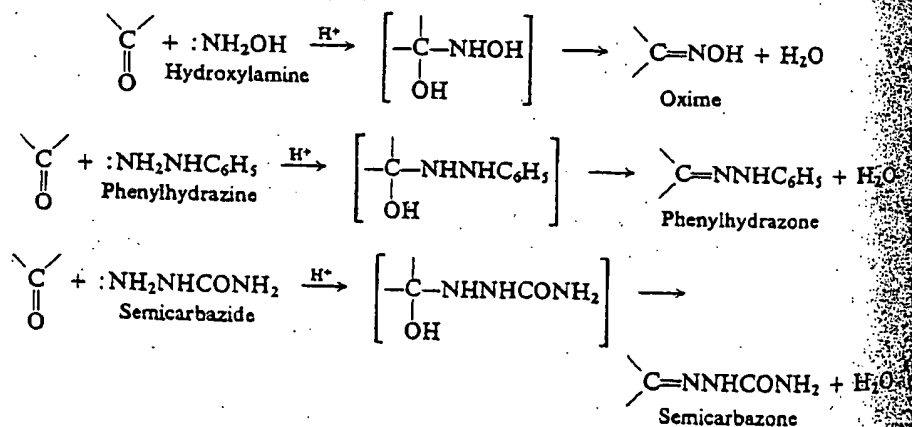


Bisulfite addition products are generally prepared for the purpose of separating a carbonyl compound from non-carbonyl compounds. The carbonyl compound can be purified by conversion into its bisulfite addition product, separation of the crystalline addition product from the non-carbonyl impurities, and subsequent regeneration of the carbonyl compound. A non-carbonyl compound can be freed of carbonyl impurities by washing it with aqueous sodium bisulfite; any contaminating aldehyde or ketone is converted into its bisulfite addition product which, being somewhat soluble in water, dissolves in the aqueous layer.

Problem 19.8 Suggest a practical situation that might arise in the laboratory in which you would need to (a) separate an aldehyde from undesired non-carbonyl materials; (b) remove an aldehyde that is contaminating a non-carbonyl compound. Describe how you could carry out the separations, telling exactly what you would do and see.

19.16 Addition of derivatives of ammonia

Certain compounds related to ammonia add to the carbonyl group to form derivatives that are important chiefly for the characterization and identification of aldehydes and ketones (Sec. 19.19). The products contain a carbon-nitrogen double bond resulting from elimination of a molecule of water from the initial addition products. Some of these reagents and their products are:



Like ammonia, these derivatives of ammonia are basic, and therefore react with acids to form salts: hydroxylamine hydrochloride, $\text{HONH}_3^+\text{Cl}^-$; phenylhydrazine hydrochloride, $\text{C}_6\text{H}_5\text{NHNH}_3^+\text{Cl}^-$; and semicarbazide hydrochloride, $\text{NH}_2\text{CONHNH}_3^+\text{Cl}^-$. The salts are less easily oxidized by air than the free bases, and it is in this form that the reagents are best preserved and handled. When needed, the basic reagents are liberated from their salts in the presence of the carbonyl compound by addition of a base, usually sodium acetate.

